

## Sturge-Weber Syndrome Research Update 2019

### RESEARCH STUDY SUMMARY:

#### Epidiolex Drug Trial

The second Epidiolex drug trial for cognitive impairments is underway with all slots filled. This trial will evaluate pharmaceutical grade Epidiolex for cognitive and social issues, migraines and motor impairments and will run for the next year. Because our prior trial of Epidiolex for medically refractory epilepsy was successful, we have been able to get patients with SWS and severe seizures on Epidiolex. Please contact Dr. Comi if you'd like to learn more.

#### Sirolimus Drug Trial

We are currently analyzing the Sirolimus trial data. The results suggest that this drug (an mTOR inhibitor and open label drug for cognitive impairment) helps a subset of patients with SWS. We are planning a follow-up trial and working to obtain funding. This is the first targeted drug treatment trial for SWS.

#### SWS Tissue Analysis

The Comi laboratory continues to work with human SWS tissue in collaboration with a Johns Hopkins scientist. We have determined that proteins downstream of mutant GNAQ (the cause of SWS) have increased activity in the abnormal blood vessels on the surface of the brain and in brain cells. These proteins are targeted by Sirolimus treatment.

#### Mouse Model

Work continues on development of a mouse model of SWS, a difficult yet important step in testing potential drug therapies and treatments prior to clinical trials. Mouse colonies with the GNAQ mutation have been established, as evidenced by DNA sequencing. Efforts to optimize conditions for the development of vascular malformations continue. Since the discovery of the underlying somatic mutation that causes SWS, developing an animal model has become a primary goal. Modeling SWS has been complicated although we knew it would be as standard genetic mouse model approaches do not work for somatic mutations.

### PAPER SUMMARY:

**Presymptomatic treatment of Sturge-Weber Syndrome With Aspirin and Antiepileptic Drugs May Delay Seizure Onset.** Pediatr Neurol. 2018 Nov 24.

This study is being utilized by other groups around the world to work on developing pre-symptomatic treatments as an approach to treating babies with SWS. We will embark on an updated study and continue to develop this approach with promising results.

**Quality of Life in Children with Sturge-Weber Syndrome.** Pediatr Neurol. 2019 Dec 10.

This study showed that patients with SWS had a lower cognitive quality of life and males had a lower cognitive quality of life than females. Younger age of seizure onset was associated with lower cognitive quality of life, as was extent of brain, skin and eye SWS involvement. Because cognitive impairment is an important determinant of quality of life in patients with SWS, we have been targeting cognitive impairment in our drug trials.

**Physical and Family History Variables Associated With Neurological and Cognitive Development in Sturge-Weber Syndrome.** Pediatr Neurol. 2019 Jul.

This multi-centered study of 277 subjects led by Kennedy Krieger determined that bilateral SWS brain involvement was associated with both learning disorder and intellectual disability, whereas port-wine birthmark extent was associated with epilepsy and an increased likelihood of glaucoma surgery. Subjects with family history of vascular birthmarks were more likely to report symptomatic strokes, and family history of seizures was associated with earlier seizure onset. Learning disorder, intellectual disability, stroke-like episodes, symptomatic stroke, hemiparesis, visual field deficit, and brain surgery were all significantly associated with earlier onset of seizures. These results are important for providing prognosis for infants and young children with SWS.

Manuscripts for the following studies are being prepared:

- MRI brain imaging in SWS study
- Medication in SWS
- Reading disabilities in SWS
- Suicidality in SWS
- Vitamins in SWS

*We look forward to keeping you updated on our progress!*

If you would like more information about research studies, please contact Dr. Comi at 443-923-9569 or via email at [comi@kennedykrieger.org](mailto:comi@kennedykrieger.org).

